Case Report

Cystic Fibrosis with a Unusual Presentation in Monozygotic Twins

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ABSTRACT

Cystic fibrosis is an inheritant autosomal recessive disease. It is associated with mutations in Cystic Fibrosis Trans Regulator gene (CFTR) and has different presentations. We report two 2 month old female patients, products of a twin delivery presented with anemia, edema, hypoalbuminemia and pneumonia. After some work ups, diagnosis of cystic fibrosis was confirmed. This is an uncommon and interesting presentation of cystic fibrosis, which occurred simultaneously in one twin.

Keywords: Cystic fibrosis, Monozygotic Twins, Autosomal recessive

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INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disease. The responsible gene is located on chromosome 7. There are multiple mutations; the most common one is delta F 508. CF has variable presentations including chronic lung disease, exocrine pancreatic insufficiency, nasal polyposis, pansinusitis, rectal prolapse, pancreatitis, cholelithiasis and insulin dependent diabetes mellitus. It also causes salt depletion. Neonates may present with cholestasis, meconium ileus and meconium plug syndrome and later in life with cirrhosis or other hepatic dysfunction. The other presentation mostly in infant is CF syndrome with triad of hypoalbuminemia, edema, and anemia. This syndrome rarely occurs simultaneously in monozygotic twins. We report one twins admitted in pediatric GI ward with CF syndrome, lung disease and mild liver involvement at the same time.

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CASE REPORT

These are two monozygotic full term female twins, who were fed with breast feeding and formula. They were referred with chief complaint of cough and respiratory distress. They had good appetite and correct feeding, but no significant weight gain after two months. Birth weight, height and head circumferences for twin 1 were 3100 g, 48 cm, and 33.2 cm, respectively, and for twin 2 were 3000 g, 49cm and 33.5 cm, respectively. On physical examination, both infants were severely pale and had respiratory distress. Weight, height and head circumference on admission were 3600 g, 52 cm and 37 cm for twin 1, respectively,

and 3500 g , 52cm and 37.5 cm for twin 2, respectively. For twin 1 and 2, temperature was 37.3°C and 36.9°C, respectively, pulse rate was 120 and 127/min, respectively, and respiratory rate was 85 and 78/min, respectively. Both twins had pale conjunctivae, buccal mucosa and round faces. Heart examination of twin 1 was normal but twin 2 had a systolic murmur grade 3/6 at left sternal border, 2nd intercostal space. Both infants had intercostal and subcostal retractions, rales and expiratory wheeze. Both had hepatomegaly, about 3-3.5 cm below costal margin, soft, with a liver span of 7-8 cm. They had 3+ pitting edema of upper and lower extremities. Symptoms of the second twin were a little milder. CXR of the first twin showed mild hyperaeration, and of the second twin, pneumonic infiltration of upper pole of right lung. Echocardiography demonstrated small Patent Foramen Ovale (PFO). Abdominal sonography of the first twin showed mild hepatomegaly with increased parenchymal echo and of the second twin, top normal liver size and few echogenic hyperechoic areas in the lower pole of right kidney, but 24 hours crystals was normal. Both twins had severe anemia and hypoproteinemia (Table 1).

Table 1: Lab Data of Two Twins on Admission

Lab-Data	twin1	twin2
Hb g/dl	4.4	5.9
WBC (mm^3)	13100	7600
Total protein - Albumin(g/l)	4.1 - 1.2	4.5 - 1.5
ALT (IU/l)	12	12
AST (IU/l)	12	51
Total Bilirubin - Direct Bilirubin	4.8 - 0.7	5.3 - 0.9
Triglyceride/Cholesterol	148/172	158/182
Prothrombin time (PT) (seconds) - Activity (%)	13 - 100%	13.4 - 92%
Alkaline Phosphatase	1088	920
Na - K (meq/l)	130 - 4.6	138 - 4.1
Sputum culture	Pseudomonas	Normal flora
Urine Protein	Negative	Negative
Stool (Occult Blood) OB	Negative	Negative
Sweat chloride (first)	130	100
Sweat chloride test (second)	120	80
Stool trypsin activity	<1/6	<1/6
Fat droplet	>100	>100

There was no proteinuria. RBC transfusion was done for them because of severe anemia; and hypoalbuminemia was corrected by albumin administration. After resolution of edema, sweat chloride test was done for both twins two times which were positive. Treatment with IV antibiotics, ventolin nebulizer, oral pancreatic enzymes and chest physiotherapy was continued and they discharged from hospital in good condition while they had weight gain too. At the age of 9 month, they had relatively good growth (their weight were 7.300 and 7.500 g, respectively). Their lung diseases were under control, and hepatomegaly was improved with proper nutrition and pancreatic extract (creon) administration.

DISCUSSION

Cystic Fibrosis is an autosomal recessive disease reported in 1/3500 live births. This is the most common life threatening genetic disease in white population. (1), CF gene codes protein CFTR of 1480 amino acids. CF has multiple mutations, the most common one is delta F-508. Dysfunction of epithelialized surfaces is responsible for broad, variable presenting symptoms and manifestations. (1), CF has variable presentations including Gastrointestional manifestations, Failure to thrive (FTT) and malabsorption, chronic respiratory disease, acid-base and electrolyte disturbance, infertility in men and dermatologic manifestations. (2,3)

One uncommon presentation of CF is CF syndrome (triad of hypoalbuminemia, edema and anemia). It may be accompanied with acrodermatitis enteropathica, hepatomegaly and elevation of transaminases. This clinical syndrome usually presents in the first 6 months of life and is associated with high mortality and morbidity. (4,5), This is an uncommon presentation of CF. There are few reports of this syndrome in each of identical twins. (6,7), In one study from the United States 47 monozygotic

and 10 dizygotic twin pairs with cystic fibrosis (not exclusively CF syndrome) were reported. (8), This study showed that cystic fibrosis can occur in twins mostly in monozygotics and rarely in dizygotics. (5), They demonstrated variable presentations such as CF syndrome (5) meconium peritonitis (9), diabetes mellitus and idiopathic pulmonary fibrosis. (10)

We report hypoproteinemia, edema and anemia in monozygotic twins that presented at the same time, when they were 2 month old and admitted in GI Ward, simultaneously. The cause of hypoalbuminemia and edema is protein malabsorption; and the cause of anemia is vitamin E deficiency and hemolysis due to fat malabsorption. (11), One way for diagnosis is sweat chloride test. Edema may result in false negative sweat chloride test; so, this test must be done after resolution of edema. (1), Treatment includes providing adequate nutrition, replacement of pancreatic enzymes, fat soluble vitamins and if needed, albumin and diuretic therapy. (12), Soy-based formula is contraindicated because soy protein has low value and causes edema in these infants. Mothers can continue breast feeding, although standard milk formula achieves near normal growth parameters.

CONCLUSION

One uncommon presentation of CF id CF syndrome (triad of hypoalbuminemia, edema and anemia). It may be accompanied with acrodermatitis enteropathica, hepatomegaly and elevation of transaminases. This syndrome usually presents in the first 6 months of life and is associated with high mortality and morbidity.

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